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STERNE, KESSLER, GOLDSTEIN & FOX, P.L.L.C. 1100 NEW YORK AVE., N.W. WASHINGTON, DC 20005			KELLY, ROBERT M	
			ART UNIT	PAPER NUMBER
			1633	

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/618,299	Applicant(s) BARSOUM ET AL.	
	Examiner Robert M. Kelly	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,34-39,41-49 and 52-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,34-39,41-49 and 52-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's response and amendments of 1/30/06 has been entered.

Claims 1, 34, 36-37, 43-45, 47-48, 52-53 have been amended.

Claims 40 and 50-51 have been cancelled.

Claims 1, 34-39, 41-49, 52-54 are presently pending and considered.

Claim Status, Cancelled Claims

In light of Applicant's cancellation of claims 40 and 50-51, all objections and/or rejections of such claims are rendered moot, and thus are withdrawn.

Drawings

In light of Applicant's amendment to Figure 6, to include the proper designations of 6A-6E, the objection to the drawings is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of Applicant's amendments, the rejections of Claims 47-48 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn.

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Claim Rejections - 35 USC § 112 – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

While the previous rejections of Claims 34-37, 39, 41-42, 44-49, and 52-53 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, are withdrawn;

Claims 34-36, 39, 41-42, 44-49, 52-53 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons necessitated by the amendments. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims encompass a generic agent that decreases uptake of a generic viral vector by kupffer cells.

The specification discloses broadly that a generic agent that saturates the viral uptake capacity of kupffer cells can be used (p. 3, paragraph 1). However, this is in the context of Applicant's finding that low doses of adenoviruses can result in increased expression of subsequently, or concurrently delivered, adenovirus comprising a transgene (p. 2, paragraph 2). The mechanism of such adenoviral action is not understood by Applicant, as they do not wish to be bound by any theory (Id., paragraph 3). Moreover, Applicant envisions the other already-known agents that deplete the amount of kupffer cells (p. 3, paragraph 3). However, Applicant has not demonstrated any other generic agent aside from the adenoviral vector and those already

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known in the art to bring about the effect desired. Moreover, no art of record demonstrates that any other agent could produce similar effects. Hence, Applicant did not possess a generic agent that reduces the ability of kupffer cells to uptake any viral vector.

Response to Argument – written description

It is noted that the rejection has been changed and Applicant is enabled for a generic agent that reduces the levels of Kupffer cells, as it is well known in the art that liposome-encapsulated cytotoxic agents are preferentially taken up by Kupffer cells when administered intravenously, thereby killing those cells, and allowing increased gene transfer of subsequently delivered adenovirus (e.g., Wolff, et al. (1997) J. Virol., 71(1): 624-29). Hence, only relevant arguments are addressed below.

Applicant's argument of 1/30/06 has been fully considered but is not found persuasive.

Applicant argues that the specification describes broadly that viral vectors, viral nucleic acids, viral particles encoding reporter genes, and particulate matter are described, and such is sufficient description for possession of the genera (Applicant's argument of 1/30/06, pp. 14-15, paragraph bridging).

Such is not persuasive. Applicant's broad description is taken in light of the disclosure that Applicant doesn't understand why or how the mechanism work, and Applicant's specification only provides speculation, which Applicant does not wish to be bound by. Hence, mere description, without any linked cause and effect, does not provide possession beyond that specifically shown, the use of adenoviruses to increase the transformation of more adenovirus encoding a transgene. Hence, possession would not be found by the Artisan.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 38-46, and 52-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

(i) a method for increasing the level of a therapeutic gene product in the liver of a subject, the method comprising administering to said subject a first adenoviral vector comprising a heterologous transgene encoding said therapeutic transgene product, operably linked to expression control elements for expression in hepatocytes and a second adenoviral vector that does not comprise said transgene, wherein said second adenoviral vector is administered prior to, or concurrently with, said first adenoviral vector, wherein the second adenoviral vector is administered intravenously, intraperitoneally, or directly to the liver;

(ii) a method for increasing the level of a therapeutic gene product in the liver of a subject, the method comprising administering to said subject a first adenoviral vector comprising a heterologous transgene encoding said therapeutic transgene product, operably linked to expression control elements for expression in hepatocytes and a liposome encapsulated cytotoxic agent, wherein said liposome encapsulated cytotoxic agent is administered prior to, or

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concurrently with, said first adenoviral vector, wherein the liposome-encapsulated cytotoxic agent is administered intravenously, intraperitoneally, or directly to the liver; and

(iii) a pharmaceutical composition comprising an adenovirus encoding a therapeutic gene product encoding a therapeutic transgene operably linked to expression control elements for expression in liver cells, a second adenovirus not encoding such transgene, and a pharmaceutically-acceptable carrier,

does not reasonably provide enablement for increasing gene product levels in any tissue other than liver, any viral vector for modulating Kupffer cell function, any viral vector for transforming liver cells, any method of administration, administration of any viral nucleic acid, the transformation of any tissue, or any agent that depletes Kupffer cells, for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Note – widened scope of enablement

Applicant's scope has been widened to allow any administration of adenoviral vectors encoding the transgene. Dr. Parr's evidence demonstrates that any vector which is administered may enter the circulation, and the Examiner has no reason to doubt that any other route would work. However, the adenovirus without the transgene must be administered by the routes given, as the Kupffer cells must be sufficiently depleted, to allow subsequent increased transformation of non-Kupffer cells. Moreover, Applicant has enablement for liposome-encapsulated cytotoxic agents, because the Art teaches, as is shown in the prior official action, that these would work.

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However, for any other particle, or virus, it remains not reasonably predictable for reasons of record.

It is further noted that the agents that are now encompassed by Applicant's claims, i.e., those that kill of Kupffer cells, must be limited to those already known in the art, as Applicant's specification only teaches one well-known compound, liposomally-encapsulated chloronidate, and the Art teaches other cytotoxic agents, as long as they are liposomally-encapsulated (e.g., Rooijen, et al. (1996) Hepatology, 23(5): 1239-43, ABSTRACT). However, nowhere does the art teach depletion of such cells via other particles of any size range, or any other compound, by any other form of administration. Hence, it would be undue experimentation to find those other compounds that work.

Response to Argument – Enablement

Applicant's argument of 1/30/06 has been fully considered but is not found persuasive.

Applicant argues that the fact that the spleen, kidney, and lung exhibited low levels of transgene expression upon intravenous injection of high levels of adenovirus (SPECIFICATION, p. 33, paragraph 2) and subsequent removal of the spleen had no effect on liver expression (p. 34, paragraph 2), that any tissue could be transformed by the adenovirus (Applicant's argument of 1/30/06, p. 18).

Such is not persuasive. Applicant is not just claiming transformation of any tissue.

Applicant's claims are drawn to increasing the level of therapeutic transgene expression in any tissue, by affecting kupffer cells. Applicant's experiments simply show that through the method of administration (I.V.), a low level of expression was seen in spleen, liver, and kidney.

Applicant's further removal of spleen did not demonstrate increased expression in any tissue, or

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even in liver. Moreover, such experiments do not demonstrate that any other tissue exhibits increased expression by acting on Kupffer cells. Hence, Applicant's argument appears to have nothing to do with the expression being increased in any other tissue than the liver.

Applicant argues that Kupffer cells represent the largest group of fixed group of macrophages in mammalian organisms, and based on this knowledge, the Artisan could predict that by acting on Kupffer cells, that expression *could* increase in other tissues without equivalent sequestration by macrophages in other tissues (Applicant's argument of 1/30/06, pp. 18-19, paragraph bridging).

Such is not persuasive. Macrophages sequester the adenoviruses and macrophages exist in the other tissues; at least that much seems to be admitted by Applicant's argument. If they exist, regardless of whether the Kupffer cells are depleted or inactivated, those other cells would be reasonably predicted to act to sequester adenoviral vectors. If such is the case, the Artisan simply could not reasonably predict that any other tissue's expression would also be increased (Official Action of 7/29/05, p. 15, paragraph 3).

Applicant argues that their claims are not directed to uptake of any vector, but only those containing a therapeutic transgene (Applicant's argument of 1/30/06, p. 19, paragraph 2).

Such is not persuasive. It is clear from the official action that the Examiner is arguing that Applicant's claims encompass any viral vector that contains a transgene, and Applicant's attempt to color the argument is not persuasive. (Official Action of 7/29/05, p. 9, paragraph 1.) In the context of addressing the vector, the Examiner may have used the term "any vector" but in the context of the whole of the Enablement rejection, it is clear that the Examiner is addressing viral vectors containing a transgene.

Applicant argues that the term “uptake” in the context of viral vectors uptaken by Kupffer cells naturally limits their claimed invention to those that are uptaken, and therefore is limited to those vectors that will work (Applicant’s argument of 1/30/06, p. 9, paragraph 2).

Such is not persuasive. The Artisan did not understand, nor does he presently understand, that there is a well-recognized genera of viral vectors that are exhibit “uptake” by Kupffer cells. No Art of record indicates such. At best, Applicant may argue that the history of this Art is generally directed to adenoviral vectors, but if such is the case, why hasn’t Applicant limited the claims to Adenoviral vectors? To wit, the Artisan has to be reasonably appraised of the subject matter which would be considered infringing. Applicant’s claimed subject matter encompasses any viral vector, not just adenoviruses.

Applicant argues that it would not be undue experimentation to determine which vectors would work in the invention, as the experimentation is considered by Applicant to be routine (Applicant’s argument of 7/30/06, pp. 19-20, paragraph bridging).

Such is not persuasive. Given the analysis of the Wands factors, it is not reasonably predictable that any virus would work in the first place, and therefore, such experimentation would be required to predict any embodiment beyond adenoviruses and liver cells, and as such would amount to inventing the claimed subject matter for Applicant. Hence, the Experimentation is undue. To wit, any experimentation would be considered routine in the Art, according to Applicant’s analysis, and as such all claimed subject matter should be enabled. Such is simply not the case. With regard to the side argument that the particles are limited in size to 70-100 nm being without support, Applicant has only shown one substance which reduces the ability of Kupffer cells to uptake a single type of vector: adenovirus vectors, and such

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substance is itself an adenoviral vector. Moreover, Applicant has already shown that they do not understand why such method works, but is also arguing that they have provided the Artisan with enablement for any substance which works. Such has given way to the written description rejection above, and necessarily requires undue experimentation has been argued, because it amounts to inventing Applicant's claimed subject matter for Applicant.

Applicant argues that the specification teaches local and systemic administration, and therefore, the claims are limited to local or systemic administration (Applicant's argument of 1/30/06, p. 20, paragraph 2).

Such is not persuasive. Applicant's claims are drawn to any form of administration, and the specification is not limiting on the terminology of the claims. Further the specification also teaches, in the same quoted paragraph, oral, nasal, parenteral, transdermal, subcutaneous or topical, and further such terminology is not written in limiting language, but in inclusive language to include any form of administration (SPECIFICATION, p. 18, paragraph 2).

Applicant argues, through post-filing evidence of Dr. Parr, indicating that subcutaneous administration of adenoviral vectors resulted in some expression of a luciferase transgene in liver, that any route of administration may be used to deliver the agents to the liver, and that expression would be increased in the liver (Applicant's argument of 1/30/06, pp. 20-21, paragraph bridging).

Such is partially persuasive. As the Examiner cannot make an argument that the adenoviral vector would not enter circulation and be taken up by liver cells, the scope of enablement has been increased to allow any administration of the adenoviral vector, however the agent that is administered to affect kupffer cell levels or affect the ability of such kupffer cells to

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uptake a viral nucleic acid with a transgene, must still be administered intraperitoneally, intravenously, or directly to the liver. The reasoning is that given in the previous official action: the uptake of such agents by the cells local to the injection site would preclude a reasonable predictability that enough of the Kupffer cells would be affected (e.g., Official Action of 7/29/05, p. 13, paragraph 2) to effect increased subsequent infection of cells of the liver. However, the injection of the adenovirus with the transgene may be by any route known in the art to effect liver transduction.

Applicant argues that the Art demonstrates that other viruses enter Kupffer cells (i.e., Dengue virus), and do so through, more commonly, non-specific uptake, than specific uptake, that the Artisan would not find reason to doubt that any virus may be used, and the Examiner has failed to demonstrate any reason to doubt it would work for anything that enters through non-specific uptake (Applicant's argument of 1/30/06, p. 23, paragraph 1).

Such is not persuasive. The Examiner has noted that Applicant has already demonstrated that they do not know the mechanism of the adenovirus in causing increased expression, and Applicant is merely speculating on the use of non-specific routes of uptake (Official Action of 7/29/05, pp. 18-19, paragraph bridging). Hence, it would be undue experimentation, amounting to inventing Applicant's invention for Applicant, for the Artisan to determine if non-specific uptake of any particular particle or virus would similarly cause such increased transformation of non-kupffer cells in the liver. Such has already been argued by the Examiner (Official Action of 7/29/05, p. 19, paragraph 2).

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Applicant argues that the Lieber paper does not demonstrate that a toxic transgene's toxicity cannot be altered by the method, as the liver tissue was shown to be growing (Applicant's argument of 1/30/06, pp. 24-25).

Such is not persuasive. The same paper and citation within that paper, p. 8805, col. 1, paragraph 3, demonstrates that there existed concern in the Artisan's mind that the high IL-6 level may be stimulating CTL activation and infiltration, which may more than make up for the action of TNF. Moreover, this is not relevant to the point made by the Examiner. The point being made is that Lieber is showing that the toxicity is not associated with the transgene, but with the virus itself (Id.). Such is followed by the showing that ricin expression is not reasonably predicted to be made less toxic as a result of Applicant's method (Official Action of 7/29/05, p. 17, paragraph 2). Hence, no toxicity of a transgene is reduced by Applicant's method, only an increased transformation of non-Kupffer cells in the liver.

Applicant argues that the expression of the transgene is being claimed, and therefore the action of ricin is not at issue, but only the action of undesirable toxicity of a transgene expression (Applicant's argument of 1/30/06, pp. 25-26, paragraph bridging).

Such is not persuasive. It is Applicant's vector which is shown to have increased levels of transformation, and not any alteration of toxicity of a transgene's expression which is shown. Applicant must claim what their invention is. Applicant has not provided any reasoning or argument to demonstrate that the toxicity of a transgene's expression is altered by their method, but only that there exists increased levels of transformation of cells in the liver and subsequent expression. If the transgene is toxic, it's toxicity is simply unaffected by Applicant's method.

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Applicant argues broadly that the laundry list is too broad, and Applicant is not required to demonstrate every working embodiment (Applicant's argument of 1/30/06, pp. 26-27, paragraph bridging).

Such is not persuasive. Applicant is required to enable the breadth of the claimed invention, and while specific embodiments may not be required to be enabled, such does not mean that whole aspects of enablement may be ignored. Applicant has not provided such breadth of enablement, such that experimentation required would not amount to inventing Applicant's claimed subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

In light of Applicant's argument, the rejections of Claims 1, 34-41, 43-46 and 52-53 under 35 U.S.C. 102(a) as being anticipated by Tao, et al. (2001) Molecular Therapy, 3(1): 28-35, are withdrawn.

To wit, Applicant's evidence that the publication was first publically available after the Applicant's priority date overcomes this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

In the light of Applicant's arguments, the rejections of Claims 34 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tao, et al. (2001) Molecular Therapy, 3(1): 28-35, are withdrawn.

Applicant's evidence that Tao is post-priority date evidence overcomes this rejection.

Because Applicant amended the claims to encompass any agent that reduces sequestration of a virus by Kupffer cells, the following rejections are necessitated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 37, 39, 41-42, 44-46 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,025,195 to Sandig, et al., and Wolff, et al. (1997) J. Virol., 71(1): 624-29.

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Sandig teaches adenoviral vectors comprising liver-therapeutic transgenes, for liver-specific gene therapy (ABSTRACT). Such vectors may be administered, *inter alia*, systemically (EXAMPLE 1), and as, they teach patients (col. 3, paragraph 6) and promoters active in man (col. 4, paragraph 7), it is also clear that the vectors are for treating humans. Moreover, such vectors are replication deficient (cols, 1-2, paragraph bridging). However, Sandig does not teach administration of an agent to decrease the uptake of the vector by Kupffer cells.

On the other hand, Wolff, as well as the art in general, recognize that many liposome-encapsulated suicide compounds, including chloronidate, may be administered 2 days before administration of the vector, in order to deplete Kupffer cells and thereby decrease uptake of subsequently-delivered adenoviral vectors (e.g., ABSTRACT).

Hence, at the time of invention, it would have been obvious to modify the method of Sandig with the liposome-chloronidate administration prior to adenovirus administration, as taught by Wolff. The Artisan would have been motivated to do so in order to increase the amount of transfection of cells. Moreover, the Artisan would have had a reasonable expectation of success, as Sandig had taught the transformation of liver with the adenovirus, and Wolff had demonstrated increased transformation of liver cells post-administration of the dichloronodate-liposomes.

Note: Claims not rejected

It is noted that certain of Applicant's claims require the prior administration of the compound to occur simultaneously or a day before administration of the vector. It is noted that Art teaches only administrations 2 or more days prior to the adenoviral vector (e.g., Wolff

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(ABOVE) and Rooijen, et al. (1996) Hepatology, 23(5): 1239-43), however, the Art does not raise any questions of doubt as to whether the administration simultaneously would be sufficient to bring about the desired effect. Hence, the claims requiring simultaneously or less than 2 days prior to administration of the vector have not been rejected. Moreover, because simultaneous administration is not obvious, the composition comprising both is not obvious.

Moreover, the toxicity of the transgene is not rejected, as it is not enabled by the art or Applicant's specification.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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